Claims: 59

1. A non-slow-binding thrombin inhibitor of the formula:

A-B-C-Lys-D

wherein

A is H, 2-hydroxy-3-cyclohexyl-propionyl-, R_1, R_1-O-CO-, R_1-CO-, R_1-SO_2-, -$(CHR_2)_nCOOR_3$, or an N-protecting group, wherein

R_1 is selected from -(1-6C)alkylene-COOH, (1-12C)alkyl, (2-12C)alkenyl, (6-14C)aryl, (7-15C)aralkyl and (8-16C)aralkenyl, the aryl group of which may be substituted with (1-6C)alkyl, (2-12C)alkoxy, hydroxy, or halogen;

R_2 is H or has the same meaning as R_1;

R_3 is selected from H, (1-12C)alkyl, (2-12C)alkenyl, (6-14C)aryl, (7-15C)aralkyl and (8-16C)aralkenyl, the aryl group of which may be substituted with (1-6C)alkyl, (2-12C)alkoxy, hydroxy, or halogen;

n is an integer of 1 to 3;

B is a bond, L-Asp or an ester derivative thereof, Leu, norLeu, -N(benzyl)-CH_2-CO-, -N(2-indane)-CH_2-CO-, D-1-Piq, D-3-Piq, D-Tiq, Atc or a D-amino acid having a hydrophobic aromatic side chain;

C is Azt, Pro, Pec, norLeu(cyclo)Gly, an amino acid of one of the formulae -N[(3-8C)cycloalkyl]-CH_2-CO- or -N(benzyl)-CH_2-CO-;

D is selected from COOH, tetrazole, oxazole, thiazole and benzothiazole;

or A and C have the aforesaid meanings, B is D-(3-8C)cycloalkylalanine, and D is tetrazole, oxazole, thiazole or benzothiazole;

or a prodrug thereof;

or a pharmaceutically acceptable salt thereof;

with the exception of the compound Me-D-Phe-Pro-Lys-COOH.

2. The non-slow-binding thrombin inhibitor of claim 1 wherein D is COOH.

3. The non-slow-binding thrombin inhibitor of claim 2 wherein A is H, (1-12C)alkyl, -CO-(7-15C)aralkyl, -SO_2-(1-12C)alkyl, -SO_2-(6-14C)aryl, or -SO_2-(7-15C)aralkyl; B is a bond, L-Asp, norLeu, D-1-Piq, or D-Phe; and C is Pro, norLeu(cyclo)Gly, or -N(cyclopentyl)-CH_2-CO-.

4. The non-slow-binding thrombin inhibitor of claim 3, wherein A is -SO_2-benzyl, B is a bond, and C is norLeu(cyclo)Gly, or wherein A is -SO_2-ethyl, B is D-Phe, and C is Pro; or wherein A is hydrogen, B is D-1-Piq, and C is Pro.

5. The non-slow-binding thrombin inhibitor of claim 1, wherein D is oxazole or thiazole.

6. The non-slow-binding thrombin inhibitor of claim 5, wherein A is H, (1-12C)alkyl, 2-hydroxy-3-cyclohexyl-propionyl-, -CO-(7-15C)aralkyl, -CO-$(CH_2)_n$COOH -SO_2-(6-14C)aryl, -SO_2-(7-15C)aralkyl, -SO_2-(1-12C)alkyl, -$(CHR_2)_n$$COOR_3$, R_2 being H or (1-12Calkyl) and R_3 being H, (1-12C)alkyl or benzyl; and C is Pro, norLeu(cyclo)Gly, or -N[(3-8C)cycloalkyl]-CH_2-CO-.

7. A process for preparing a non-slow-binding thrombin inhibitor of claim 1, the process including coupling suitably protected amino acids or amino acid analogs, followed by removing the protecting groups.

8. A pharmaceutical composition comprising the non-slow-binding thrombin inhibitor of any one of claims 1-6 and pharmaceutically acceptable auxiliaries.

9. The non-slow-binding thrombin inhibitor of any one of claims 1-6 for use in therapy.

10. Use of the non-slow-binding thrombin inhibitor of any one of claims 1-6 for the manufacture of an antithrombotic medicament.